

soap and sudden changes in temperature, and proper ointments play as important a rôle as the various allergens.

I believe it particularly wise to reassert the value of the skin test and individual study. While granting the variability of the former and necessity for repeated observations, it remains a most helpful guide.

Regarding dietary restrictions for growing children, I think that we should be most careful not to neglect the necessary protein requirement for growth. Animal protein is particularly desirable as a source of body protein. Sweeping restriction may produce a malnutrition most dangerous to the general health. I am not sure, for example, that a well-nourished eczematous infant is not a better risk than a malnourished, poorly resistant infant without so marked an eczema.



EDWARD MATZGER, M. D. (909 Hyde Street, San Francisco).—I congratulate Doctors Miller and Piness for again publishing on the general subject of the allergic constitution. The bulk of the contributions on allergy have to do with the discovery of new excitants, of methods of study and of types of treatment. While this information is valuable, all of us treating allergic individuals are anxious to know more about the fundamental nature of the allergic constitution. Surely a statistical compilation of large groups of allergic patients who have been observed, tested and treated over a period of years, must contribute much to our understanding of the nature of the allergic group.

As the authors so graphically emphasize, we also must realize that an asthma attack in a child is just the beginning of a long series of allergic episodes. The proper treatment of each hypersensitive manifestation will tax the physician's diagnostic acumen, and he must be alert to the early recognition of each etiologic factor.

A new excitant, if quickly recognized, can be eliminated from the patient's environment, or an active immunity be induced before secondary factors assume importance. This procedure may save months of suffering and often surgical intervention.

Elimination diets, in one form or another, have been used ever since mothers have observed indispositions following the ingestion of certain foods, and certainly are to be advocated wherever they can be built up clinically. Elimination diets, however, based on average skin test reactions are obviously of less importance than elimination diets based on individual skin test diagnoses.



WILLIAM W. BELFORD, M. D. (2545 Fourth Avenue, San Diego).—Our thanks are due to Doctors Miller and Piness for this paper. Those of us in the field of pediatrics are often hard-pressed to care for our asthma patients. It is likely each member of this section has seen asthma develop in a patient that has been under care for eczema. I doubt if any of us realized that the percentage of eczema patients later developing asthma was so large.

I am sure that the frequency of nasal symptoms of an allergic condition is not generally recognized. The frequent "colds," insignificant as they often are, yet quite a bother to the parent, with itching and frequent sneezing, are perhaps as common complaints as any that we hear of in the whole field of allergy. All too often we forget the allergic possibility until asthma or some other equally striking manifestation of the child's extreme sensitivity appears.

In the well-developed allergic rhinitis, eosinophils are found readily enough on study of a nasal smear. The same is true of a careful study of a series of blood smears when an elevation of the eosinophil count is very frequently found. In the early case (and each has to begin some time) this eosinophilia is not so common.

It seems that the scratch tests have been replaced by the intracutaneous tests. Doctors Miller and Piness

check each negative scratch test with an intracutaneous test. They find about 80 per cent of the patients sensitive. So many parents are discouraged when an accurate study of their child is proposed, because they have seen a few scratch tests done with negative results. When the tests are done properly and carefully, a vast amount of information is obtained. With sufficient study and industry on the part of the physician doing thorough allergy work, about 80 per cent of these children can be brought "into balance." A "cure" cannot be expected, as Doctor Miller most aptly points out.

DIPHTHERIA IMMUNIZATION*

By LILLIAN KOSITZA, M. D.
Los Angeles

DISCUSSION by H. E. Thelander, M. D., San Francisco; George M. Stevens, M. D., Los Angeles; A. J. Scott, Jr., M. D., Los Angeles.

IN this article will be given a brief sketch of the prevalence of diphtheria in California, with special reference to the city of Los Angeles; also an evaluation of the various immunizing agents now employed to prevent the spread of the disease.

In most large cities diphtheria prevails endemically with periods when outbreaks of considerable severity are observed.

LOS ANGELES FIGURES

Our statistics show that during the decade 1921-1931 the diphtheria rate in Los Angeles steadily dropped. In the incomplete fiscal year 1931-1932 an increase in the number of cases and deaths has been noted.

The rates on the basis of one hundred thousand population are as follows:

TABLE 1.—Los Angeles Figures for Ten-Year Period

Fiscal Year	Case Rate	Death Rate
1921-1922	355	15.6
1930-1931	64	5.6
1931-1932 (estimated).....	105	7.04
Cases to date, total.....986		Deaths to date, total.....66

Morbidity figures for the state since 1923 show between 55 to 60 per cent of cases occurring in children under ten years of age. State figures, likewise, indicate that the fatality per cent is greatest in the preschool group. Morbidity and fatality per cent in age groups for children throughout the state are available since 1928.

Our own figures for Los Angeles City for 1931 show that fifty-four deaths out of a total of seventy-one occurred in children under ten years of age.

From analysis of the above figures we must conclude that the morbidity is greatest in the age group five to nine years, but that the danger to life is greatest in infants and the preschool group. We therefore cannot sufficiently stress the importance of protecting the preschool children from the dangers of diphtheria.

A recent report by Kinnaman¹ on the status of diphtheria in the State of Kansas indicates that

* Read before the California Lutheran Hospital staff, April 19, 1932.

TABLE 2.—*State Morbidity and Fatality Figures*

Age Group	1928		1929		1930		1931	
	Cases	Fatality	Cases	Fatality	Cases	Fatality	Cases	Fatality
Under 1 year	88	14.8%	40	17.5%	50	30%	42	19%
1-4 years	974	10.6%	615	12%	641	10.3%	686	12.2%
5-9 years	1703	5.9%	1059	7.1%	1063	6.3%	1328	4%

there was state-wide culturing of twenty thousand school children, whereby it was found that the per cent of carriers was practically the same in the immunized group as in the nonimmunized group. Furthermore, the immunized group were carriers of organisms of the most virulent type. From these observations they concluded that their case-fatality rate is increasing in the nonimmunized group, who contract diphtheria through exposure to these immunized carriers. It would appear then that in a partially immunized community there is greater danger to the nonimmunized group. This is a point to consider with regard to our own increased morbidity and fatality rates this year.

DIPHTHERIA IMMUNIZATION

That diphtheria immunization has played a great part in lowering the incidence of the disease during the last decade is generally accepted. That there may be some other factor which is to some extent also responsible for this decreased incidence cannot be denied.

Not until 1894, when Behring of Germany and Roux of France discussed antitoxin at an international congress in Europe, was there any known remedy for diphtheria. Following this congress, its use was begun in New York City by Park and Biggs,^{2,3} who began using it in the treatment of diphtheria and also as a preventive in those exposed. It was soon shown, however, that antitoxin could not be relied upon as a means of stamping out diphtheria.

Behring, about 1914, published results on toxin antitoxin as an immunizing agent in man. The progress of his work was interrupted by the World War. About this same time Schick demonstrated the value of the Schick test in determining susceptibility to diphtheria. Park and Zingher were the first to utilize the Schick test in determining the difference in reaction before and after administration of toxin antitoxin in susceptible children. By far the greatest amount of immunization work with toxin antitoxin was done in this country by Park and Zingher in New York City, where a city-wide effort to stamp out diphtheria began in 1920.

The first preparation of toxin antitoxin was made from undiluted toxin to which was added a certain amount of antitoxin. This at times caused severe local and general reactions. As time went on, diluted toxin, slightly more underneutralized, was used and less severe reactions followed.

By the end of 1928 fully 500,000 school children in New York City were immunized by the use of toxin antitoxin.

A campaign for prevention of diphtheria in pre-school children was then started with the result

that in a three-year period between 300,000 and 400,000 preschool children were immunized.

Within the last decade numerous reports have been published showing varying results with toxin antitoxin. Negative Schick tests following immunization have been reported in some groups above 90 per cent by Park and Zingher⁴ and in other groups by Harrison^{5,6} as low as 60 to 70 per cent.

VARIATION IN RESULTS

The variation in the results may be due to difference in potency and to some extent to difference in reactions of subjects. Those in rural and less congested districts are more refractory to immunization than those in congested urban groups, where repeated exposure to diphtheria takes place. This has also been demonstrated in orphanages and boarding schools, where Schick tests were made on large groups, showing that the longer the children remained in these institutions the more apt they were to become Schick-negative. These groups when immunized with toxin antitoxin showed a larger percentage of negative Schicks following immunization in the groups which had been in the institutions the longest time. Others regard susceptibility to diphtheria not entirely a matter of environment but as due to some hereditary factor, finding a high correlation between resistance and susceptibility of parents and children.

Some experiments indicate that a longer time interval between injections may give better results. In some cases where after one course of injections children have remained Schick-positive, one or more injections with toxin antitoxin has quickly rendered them Schick-negative. Other experimenters have tried two-week intervals with toxin antitoxin, others have recommended four doses instead of three, others still have recommended even five doses in adults. Thelander⁷ in San Francisco reported 92.3 per cent negative Schicks in a group of seventy-seven children under eighteen months of age with four injections of toxin antitoxin, whereas the previous year in a group of 115 with three injections they had 70.1 per cent negative Schicks. However, the three injections of one cubic centimeter each with toxin antitoxin at weekly intervals is the established method and has given the most satisfactory results.

TOXOID

Although in the United States toxin antitoxin has been most extensively used as an immunizing agent against diphtheria, toxoid has gained widespread popularity in France and Canada. Within the last few years, however, toxoid has been used more extensively in the United States and at

present seems to be rapidly replacing toxin anti-toxin as an immunizing agent.

Experiments with the use of toxoid (or anatoxin) by Ramon^{8, 9} in France have been carried on since 1923. This type of immunization has gained increased popularity, so that over a million people have been immunized by this method. Toxoid is prepared by adding formalin to toxin and subjecting the mixture to a temperature of about 40 degrees centigrade until all toxicity is lost, which usually takes from three to six weeks. Those advocating toxoid claim

for its superiority over toxin antitoxin because:

1. It does not cause any serum sensitization (no serum being used in its preparation). Although Park⁸ is of the opinion that the danger of serum reactions has been greatly exaggerated, it nevertheless is a factor to be considered, as shown in a detailed report by Gordon and Creswell.¹⁰ They showed that even small doses of horse serum as used in toxin antitoxin were sufficient to give serum reactions in a large number of cases when subsequent therapeutic antitoxin was administered. To overcome this difficulty toxin antitoxin from goat serum and sheep serum is now available on the market.

2. There are a greater number of children immunized by the use of toxoid, as evidenced by a greater percentage of negative Schicks. Schwartz and Janney¹¹ found that in a group of 361 immunized with three injections of toxin antitoxin they had 78 per cent negative Schicks, whereas in a group of 128 where three injections of toxoid were used they had 98 per cent negative Schicks. Weinfeld and Cooperstock¹² reported a study with 104 nurses and medical students, showing 92 per cent negative Schicks when two doses of one cubic centimeter at three-week intervals were used.

3. The immunization is produced in a shorter period of time (six weeks to three months). Harrison⁶ reports 355 children to whom three injections of toxin antitoxin were given at weekly intervals who showed 64 per cent negative Schicks three to six months later, as compared with a group of 318 children who received two doses of toxoid, one cubic centimeter each, with interval of thirty-one days between injections. In three and one-half months 94 per cent of these were Schick-negative.

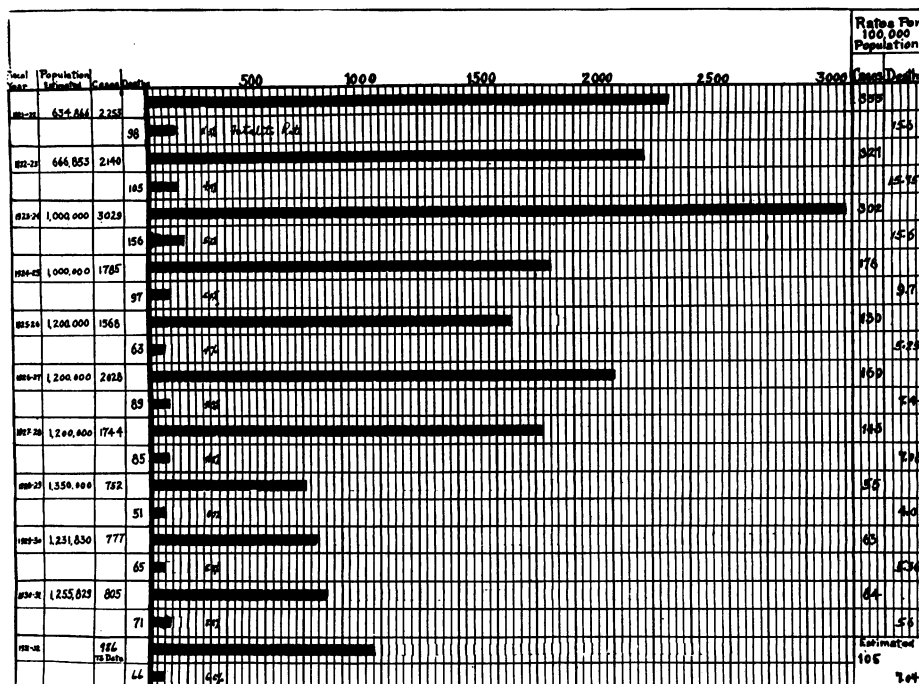


Chart 1.—Illustrates the morbidity and mortality figures for each fiscal year beginning 1922 and ending 1932.

4. Toxoid is more stable than toxin antitoxin. It does not dissociate by freezing, and therefore does not liberate free toxin, an objection frequently raised against the use of toxin antitoxin.

The chief drawback to the general use of toxoid is the severe local and general reactions which may follow its use in older children and adults. Few reactions occur in children under six years. Reactions to a large extent can be avoided by testing the individuals for reactions by using a small test dose of diluted toxoid, which is generally supplied in the package. If reactors are found, smaller doses, starting with one-tenth cubic centimeter, should be given, and as many as five smaller doses at two-week intervals may be necessary instead of the recommended two to three doses of one cubic centimeter each at varying intervals. No standardization of dosage and intervals at which toxoid should be given has as yet been established. Some recommend two doses of one cubic centimeter, varying the interval, as three weeks, one month, or six weeks between the two injections; others give three doses of one cubic centimeter at two-week intervals; others recommend variations in dosage, as .5 c. c., 1 c. c. and 1 c. c., or .5 c. c., .5 c. c. and 1 c. c. for the consecutive doses. Much has yet to be done to establish the optimum dose and optimum interval between doses. Some mention has recently been made of the use of a small amount of alum in toxoid preparations, which renders even a higher percentage immune. This preparation is as yet not generally available.

LOEWENSTEIN'S OINTMENT

Loewenstein's Ointment has recently also been tried as an immunizing agent against diphtheria. The ointment consists of toxoid and the filtered full culture of dead bacilli. Abt and Feingold¹³

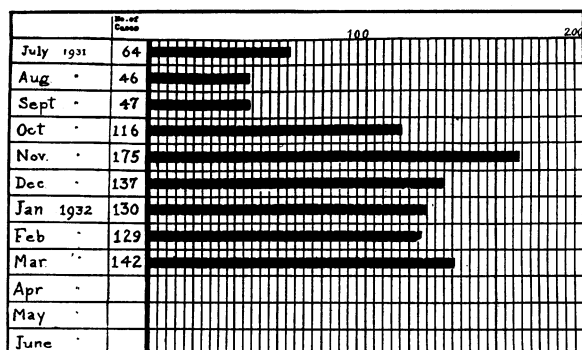


Chart 2.—Illustrates the incidence of diphtheria per month, beginning July, 1931. The increase started in October, 1931, and has continued each month through March of this year.

in this country have reported on its use in sixty-two children with resultant immunity in 70.9 per cent. Advantages claimed for it are chiefly: (1) Its use by inunction avoids the use of a needle. (2) No foreign protein is introduced. (3) It is not followed by any reactions local or general. Experiments with the use of this ointment have not been reported sufficiently to warrant any conclusions.

SCHICK TEST

No discussion of immunization is complete without some mention of the Schick test. We assume that a negative Schick test means the presence of sufficient antitoxin to neutralize the action of diphtheria toxin. This should correspond to at least one-thirtieth unit antitoxin per cubic centimeter of serum. Although a positive Schick is a reliable index that the individual has not sufficient antitoxin and is susceptible to diphtheria, a negative Schick is not correspondingly an absolute index that the individual has sufficient antitoxin to be protected. There are several sources of error which may arise from faulty technique in making a Schick test. The test must be made intracutaneously, and it is easy in some cases, especially in young children, to go below the skin. The toxin must be of proper strength and proper amount; exactly one-tenth cubic centimeter must be used. Recently there has been available Schick material where the toxin is already diluted and ready for use. This simplifies matters for a busy practitioner.

In children under six years no Schick test is necessary because the great majority under six years of age are susceptible. In our clinic practice, no routine Schick is made in children under ten years of age.

LOS ANGELES' EXPERIENCE

Diphtheria immunization with toxin antitoxin was started in Los Angeles at the Anita Baldwin Clinic in December, 1923. The next year the work was undertaken by the Los Angeles City Health Department. To date we have given approximately 136,000 injections, immunizing approximately 45,000 children, most of whom have been immunized in the last few years. Our experience has been chiefly with toxin antitoxin with most satisfactory results. We have not been able to compare the value of toxin antitoxin and toxoid by

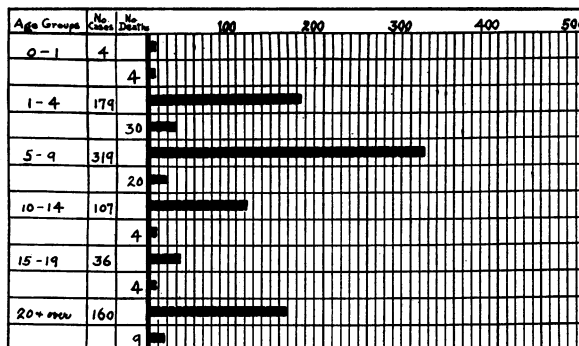


Chart 3.—Illustrates the morbidity and mortality for the different age groups for the fiscal year 1931. It is striking that 63 per cent of the cases are in children under ten years of age. Our figures further show that in 805 cases reported for 1931, 101 were in children six years of age. Our own figures, as well as those furnished us by the State Health Department, show that the highest morbidity and fatality percentage occur in the younger age groups.

the percentage of negative Schicks following the injections, but have, however, had ample opportunity to compare the two immunizing agents from the standpoint of reactions. Our work with toxoid was started in October, 1930, at one of our clinics with a preschool group. No reactions followed, and we extended its use to the public schools in January, 1931. We continued the use of toxoid in the city schools until January, 1932, immunizing about 3,600 children by this method. At this time, because of the relatively frequent reactions both local and general, and the complaints of some of the principals, we considered it better policy to limit our use of toxoid to our conferences for the preschool group and use the long-tried toxin antitoxin, which has given us relatively few reactions for the school group.

In our older school children, reactions following the use of toxoid occurred frequently, causing in many cases loss of time from school. Reactions reported were either local as characterized by swelling, redness and tenderness, or general with such symptoms as fever, headache, nausea, and vomiting. In some cases both local and general reactions were reported.

Although it is recommended that older children and adults be tested for reactions by using a small amount of diluted toxoid, such procedure was not practical in our immunization program in the school.

At present we are using toxoid for all children up to seven years of age, giving it in two injections of one cubic centimeter each at monthly intervals, and toxin antitoxin for all children over seven years of age and adults, giving it in three injections of one cubic centimeter each at weekly intervals.

CONCLUSIONS

1. Our statistics on diphtheria indicate that the greatest morbidity occurs in children five to nine years of age, and the highest fatality rate in children under five years of age. In other words, the younger the child the greater the menace of diphtheria.

2. The importance of diphtheria immunization must be stressed in the preschool child and can

safely be accomplished during the first year of life.

3. The evaluation of immunizing agents now extensively employed show advantages in the use of toxoid because it does not sensitize to serum, is more stable, does not dissociate by freezing, and produces immunity in a shorter time and in a greater percentage of cases.

4. The use of toxoid in school children has given us severe reactions, causing loss of time from school. The use of toxoid in younger children has not produced any reactions.

5. We now limit our use of toxoid to children under seven years of age, and toxin antitoxin to older children and adults.

Los Angeles City Health Department.

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DISCUSSION

H. E. THELANDER, M. D. (384 Post Street, San Francisco).—The fact that in the Los Angeles schools toxin antitoxin was discontinued in favor of the better immunizing agent, toxoid, and then returned to when the latter gave annoying reactions is sufficient evidence that the ideal method of immunizing children has not yet been reached.

In public health work, where there is not the close relationship between parents, doctors, and children that there is in private practice, it is essential in order to carry out successfully a public health program that the methods used be as far as possible above criticism. Seventy per cent immunity, which is a generous estimate for toxin antitoxin, is not sufficient security for children to warrant continuing its use without re-Schicking the children.

Diphtheria in supposedly immunized children discredits the procedure, and severe serum disease following the treatment of such cases does not simplify the problem. On the other hand, if toxoid incapacitates a fair percentage of children for a day or more with each injection it will not be accepted by the public. It is quite possible that one cubic centimeter doses of toxoid are larger than necessary. We have immunized nurses with five small doses, totaling 1.5 to 2 cubic centimeters, with satisfactory results and very slight reactions. Even smaller doses may be effective. We are at present running such a series in Schick-positive medical students.

The percentage of Schick positive adults is surprising. In recent groups we had from 40 to 80 per cent positive in nurses, medical, and dental students. Double Schicks were made on these groups, the old Schick with control material being applied to one arm, and the new already diluted material and its control to the other. Discrepancies were checked by Kellogg tests. The new material was found considerably less reliable than the old.

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GEORGE M. STEVENS, M. D. (Los Angeles City Health Department, Los Angeles).—Toxin antitoxin as a prophylactic for diphtheria will soon be obsolete; in fact it should never be used by choice on any individual. Any preparation containing horse or other serum should be reserved for treatment rather than for immunization.

Serum disease is entirely too prevalent and is not considered seriously enough. The fact that an individual may in some future disease crisis require serum antibody therapy should never be lost sight of, nor the fact that the avoidance of serum sickness at that crisis may mean the difference between life and death.

Although violent immediate reactions of serum have sometimes followed the first known injection, we know that in most instances serum has been given at some previous time.

Toxoid free from serum is rightly usurping the place of toxin antitoxin. Emphasis, of course, should be placed upon immunization of the preschool child. The slogan should be, "Protect every child at six months of age."

Toxoid reactions as they occur in older children are protein reactions, but not serum protein reactions. The objectionable substance, chiefly at least, comes from the autolyzed diphtheria bacilli of the culture in the making of the toxoid. A good product as now made is five times as potent for protective purposes as toxin antitoxin. If there is added only an equal quantity of diluent, the product is still two and one-half times stronger than toxin antitoxin and seldom gives annoying reactions and is therefore more desirable to use on older children.

The persistence of immunity in children immunized with toxoid is the same as when toxin antitoxin is used.

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A. J. SCOTT, JR., M. D. (1401 South Hope Street, Los Angeles).—Doctor Kositz has presented the subject of diphtheria immunization as it is practiced today by public health officers and pediatricians.

In our work we use one cubic centimeter of toxoid every three weeks for three doses, starting at the age of six months and up to six years of age. We find no local or constitutional reactions. We use the same dosage for the infant as for the older child. For the child past six years old we use toxin antitoxin every two weeks for three doses.

We never use the Schick test under six years of age to determine susceptibility prior to giving the toxoid, but always use the test for children over six years. We test children four to six months after the last immunizing dose. We prefer the Schick material that requires dilution at the time of use. No control is used, but we have the child return in six or seven days for reading the test. This time interval eliminates the pseudo-reactions. In order that we may be certain that the material is potent, we test a large group of children at one time and use mothers and nurses, who

have not been treated, as controls and find many times two or more of these latter will give a positive Schick reaction.

If after immunizing doses a child has a positive Schick test, we wait another ninety days, re-Schick and if still positive repeat the toxoid or toxin antitoxin, using, however, only two doses three weeks apart. We then re-Schick in another ninety days. The test is usually negative at that time.

The question of exact dosage and time interval between doses is not definitely settled yet, but until that time the present technique is workable and does no harm but much good.

It has never been our experience to see any sensitization to horse serum from the use of the toxin antitoxin, with one exception, since the first use of this material a number of years ago, and in many hundreds of immunizations. It is possible to have it occur, but this should not deter us from using the material in the older child if he is susceptible to diphtheria. This is another argument for the early immunization of the child with the toxoid.

The statistics that Doctor Kositzka presents for the Los Angeles district show that the education that has been going on for the past few years is bearing fruit. However, the gradual increase in the morbidity and mortality rates of the past two years shows that there has evidently been a letting up of the intensive campaign for diphtheria immunization on the part of ourselves as practitioners, and the work of education may be taken over by the health authorities.

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DOCTOR KOSITZA (Closing).—I wish to thank Doctors Thelander, Stevens, and Scott for discussing my paper.

Since this paper has been written we have again resumed the use of toxoid in our diphtheria immunization in the Los Angeles City schools. We are endeavoring to carefully check on the type and frequency of reactions to toxoid in children over six years of age.

THE LURE OF MEDICAL HISTORY*

FIFTY YEARS OF PROGRESS IN THE PREVENTION OF DISEASE†

By J. C. GEIGER, M. D.
San Francisco

I

THE revolution in preventive medicine, so ably begun by a chemist, the revered Louis Pasteur, was given great impetus by Ryndall, a physicist, and Robert Koch, a bacteriologist. Bacteriology has, in turn, revolutionized our isolation and quarantine procedures, particularly as to recognition of the existence of the healthy carrier. There is no doubt that Theobald Smith focused attention on the importance of transmission of disease by insects. Biggs really modernized public health practice in the United States.

It was not many years ago that the conscientious health officer first offered to quarantine the cases of communicable disease that busy practitioners happened to report. When the quarantine terminated—the time being usually set by convenience or by social standing—the premises

were diligently fumigated. Many communities expressed heartfelt gratitude for this service. But quarantine and terminal fumigation are both relatively unimportant features today in the control of communicable disease. Fumigation, with its frequent destruction of clothes, bedding, etc., was time and energy wasted.

An entirely new conception of public health arose when healthy carriers were recognized to exist, and when mild, atypical or missed cases could and did account for the spread of disease. It is now axiomatic that, if communicable diseases are to be controlled, we must investigate and determine their source and destroy it, and learn how diseases are disseminated. But in many common infectious diseases we must deal primarily with persons, not things.

There are fanciful routes of infection popularly suggested in some diseases; even now the cancer house is spoken of as was the tuberculosis house in years gone by. Diseases carried by letter are not quite in the limbo of things forgotten. Some genuine modes of transmission, in a few diseases, do stretch the plausibilities. We must provisionally accept all possibilities, but never exclude the usual routes. These are, for all practical purposes, contact, milk, and water.

The control of any disease depends, first, upon an early and accurate diagnosis; second, the source, vehicle, or avenue of infection; and third, the prompt blocking of these with every reasonable force. It depends also on public confidence in the health officer, for sometimes he must take extraordinary steps. There is no need, ordinarily, to prevent contact of persons; but drinking water and milk should be carefully analyzed before their use is permitted.

One of the difficulties here becomes acutely manifest. Much laboratory work is inconclusive; specimens examined today and found potable may tomorrow show an unhealthful condition. To make milk and water safe for human consumption means an untold number of inspections, ceaseless vigilance and a balanced understanding of the factors operating within and without the supplies. It is possible to discover an infecting organism in the water and milk, but seldom indeed is it discovered or even attempted. The most important and most difficult control is the isolation of the infected, since it is not feasible to go through the whole community. Quite often, milk handlers and others are subjected to examinations of all types, particularly of specimens of the urine, the feces, and from the throat; the value of the examinations depends upon the skill of the laboratory technician and the promptness of the investigation.

STATISTICAL EPIDEMIOLOGY

Two of the modern weapons of public health work are bacteriology and epidemiology. Many of our older health officials regard them as synonymous. But lemology, or lemography, meaning the sum of human knowledge as to pestilence, was long known before bacteriology came into existence. The term "epidemiology" is more frequently used today. Epidemiology is a science with ramifications, including occurrence, incidence, distribu-

* A Twenty-five Years Ago column, made up of excerpts from the official journal of the California Medical Association of twenty-five years ago, is printed in each issue of CALIFORNIA AND WESTERN MEDICINE. The column is one of the regular features of the Miscellany Department of CALIFORNIA AND WESTERN MEDICINE, and its page number will be found on the front cover index.

† One of a series of public lectures by invited speakers, conducted by the Stanford University School of Medicine.

‡ From the Department of Public Health, San Francisco.